Remarks

The February 25, 2003 Official Action has been carefully reviewed. In view of the amendments submitted herewith and these remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset it is noted that a shortened statutory response period of three (3) months was set forth in the February 25, 2003 Official Action. The initial due date for response, therefore, was May 23, 2003. A petition for a one month extension of the response period is presented with this response, which is being filed within the one month extension period.

In the February 25, 2003 Official Action, the Examiner notes that the application does not fully comply with the requirements of 37 C.F.R. §§1.821-1.825.

The Examiner has also objected to claims 6 and 7 for improper punctuation, and to the specification for lacking sequence identifiers, containing a non-descriptive title, and omitting a document number.

The Examiner further objects to the specification for allegedly lacking clarity in describing the origin and make-up of plasmids pJLK105 and pNTEP2 and the overall construction of plasmids pJLK136, pJLK138, pJLK140, and pJLK121.1.

The Examiner has objected to claim 19 under 37 C.F.R. §1.75(c) as being improperly dependent on more than one claim.

The Examiner has rejected claims 1, 2, 4-19, and 28 under 35 U.S.C. §112, second paragraph as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. The Examiner's reasons in support of the ground of rejection are set forth in paragraphs 13-18 of the February 25, 2003 Official Action.

Claims 1, 2, 4-19, and 28 also stand rejected under

35 U.S.C. §112, first paragraph, as the enablement provided by the specification is allegedly not commensurate in scope with the claims.

The foregoing objections and rejections constitute all of the grounds set forth in the February 25, 2003 Official Action for refusing the present application.

In accordance with the present amendments, the specification has been amended to provide appropriate sequence identifiers throughout. These amendments are believed to place the application in full compliance with 37 C.F.R. §§1.821-1.825.

The title has been amended, in accordance with the Examiner's suggestion, so as to satisfy the requirement for a title which is more descriptive of the claimed invention.

Regarding the omission of the application number of Applicants' copending international patent application referred to at page 7 of the specification, the specification has been further amended to contain the publication number of the copending international application. The application is entitled "Polyketides and their synthesis" and was filed on June 29, 1999 as indicated in the original specification.

As for the objection to claims 6 and 7 for containing improper punctuation, these claims have been amended to overcome these objections.

Applicants have also amended claim 19 by replacing the reference to claim 9 with a recitation of the subject matter of claim 9. Therefore, the objection to claim 19 under 37 C.F.R. §1.75(c) has been overcome.

Applicants have also amended claims 2-13 to better conform with claim 1 by referring to the nucleic acid **molecule** of claim 1. Applicants have also added the abbreviations used for the various reduction domains to claims 10 and 11 for clarity. Support for these amendments can be found at page 2, lines 20 and 21.

No new matter has been introduced into this

application by reason of any of the amendments presented herewith. Moreover, none of the present claim amendments is believed to constitute a surrender of any originally claimed subject matter, or a narrowing of the claims in order to establish patentability. The effect of these amendments is merely to make explicit that which was implicit in the claims as originally worded.

For reasons set forth below, Applicants respectfully submit the lack of clarity objection regarding the origin, make-up, and overall construction of various plasmids, and the 35 U.S.C. §112, first and second paragraph rejections of claims 1, 2, 4-19, and 28, as set forth in the February 25, 2003 Official Action, either lack merit or cannot be maintained in view of the present amendments. These grounds of objection and rejection are, therefore, respectfully traversed.

THE SPECIFICATION PROVIDES A CLEAR DESCRIPTION OF THE CONSTRUCTION OF PLASMIDS pJLK05, pNTEP2, pJLK136, pJLK138, pJLK140, and pJLK121.1

The Examiner's objection to the specification, for allegedly not clearly describing the origin and make-up of plasmids pJLK05 and pNTEP2 at page 15, line 27 and the overall construction of plasmids pJLK136, pJLK138, pJLK140, and pJLK121.1 at pages 39-45, is unfounded.

Applicants note that each of the aforementioned plasmids is described by citation to a reference or is synthesized by the use of a plasmid or cosmid that is described by citation to a reference. Specifically, plasmid pJLK05 is synthesized in part from plasmid pJLK01 which was described in the PCT/GB97/01819 application (see page 15, lines 14-22). Plasmid pNTEP2 is described by reference to Oliynyk *et al.* and application WO98/01546 (see page 14, lines 11-13).

Plasmids pJLK136, pJLK138, and pJLK140 are all

synthesized, in part, from plasmid pWHM3 which is described in Vara *et al.* (see page 39, lines 19-21). Additionally, plasmid pJLK121.1, which is described in detail at page 26, line 22 through page 27, line 6, is synthesized, in part, from cosmid cos 26 described in Schwecke *et al.* and from plasmid pUC18 which is a common commercially available plasmid available from, for example, Amersham Biosciences (Piscataway, NJ). Applicants respectfully submit that a skilled artisan would be able to readily obtain the referenced manuscripts and patent applications and with the information provided thereby carry out the construction of the plasmids in question. However, Applicants are prepared to add the description of the plasmids from the various patent applications and manuscripts to the present specification, if required by the Examiner, as the publications are all incorporated by reference into the instant application (page 57, lines 14-16).

CLAIMS 1, 2, 4-13, 18, 19, AND 28 AS AMENDED AND CLAIMS 14-17 FULLY SATISFY THE REQUIREMENTS OF 35 U.S.C. 112, SECOND PARAGRAPH

In support of the 35 U.S.C. §112, second paragraph rejection of claims 1, 2, 4-19, and 28 the Examiner asserts that claim 1 is difficult to understand in its original composition with specific reference to the use of the phrase "at least part of." The Examiner also contends that claims 1, 2, 4-19, and 28 are confusing, in the absence of a requirement that the polylinker region encode a "read-through" sequence "so as not to impede translation of the full peptide."

Applicants have adopted the substance of the Examiner's helpful suggestions in the present claim amendments. Thus, claim 1 has been amended to replace the phrase "at least part of" with the term "modified." Additionally, claim 1 has been amended to recite that the polylinker be in an in-frame insertion into the polyketide synthase (PKS) gene. Applicants submit that such an amendment

eliminates what the Examiner perceives as an ambiguity in the claim, as an "in-frame insertion" of the polylinker will allow for the proper continuation of the translation of the gene. Support for this amendment of claim 1 is provided in the specification at, for example, Figure 4 and page 16, line 1 through page 17, line 13 wherein a PKS gene containing the synthetic polylinker provided in Figure 4 is determined to be functional. Inspection of the sequence of the synthetic polylinker provided in Figure 4 reveals that the polylinker has not induced a frameshift upon insertion into the PKS gene by AvrII and HpaI digestion (i.e. it was inserted in-frame).

The Examiner also contends that the terms "uncommon" and "some" render claim 5 indefinite. Applicants have again employed the Examiner's helpful suggestion in amending claim 5 to recite "at least one" instead of "at least some." Additionally, the term "uncommon" has been replaced with citation to restriction sites that are "absent from at least about half of" other known naturally occurring nucleic acid sequences encoding reductive enzymes. Support for this amendment can be found in the present specification at page 7, lines 9-21.

According to the Examiner, claims 5, 9-13, 18, and 19 are additionally unclear for reference to "reductive enzymes" as reduction is performed by domains and not enzymes in the PKS field. Applicants have accordingly amended the indicated claims to recite reductive domains instead of enzymes.

The Examiner has additionally characterized the subject matter of claims 9-13, 18, and 19 as "wholly confusing as to its usefulness." In this connection, the Examiner appears to doubt the utility of replacing a deleted reduction domain with the same reduction domain inserted into the introduced polylinker. Applicants respectfully submit that there are numerous reasons for inserting the same domain that was deleted into the polylinker region. For example, a

skilled artisan would readily appreciate that the insertion of the deleted domain into the polylinker would serve as a control against which other inserted reduction domains can be compared. Moreover, as noted in the present specification at page 11, line 25 to page 12, line 17, the placement of a domain at two different restriction sites yielded two different products. Therefore, a skilled artisan would appreciate that the removal of a reduction domain and replacing the same reduction domain in an altered context (i.e. the polylinker) is capable of producing different products. Applicants also emphasize that claim 1, as amended, recites replacing at least one reduction domain with a polylinker. A skilled artisan would appreciate that the replacement of one of two removed reduction domains, for example, could have significantly different effects on the PKS product. Therefore, Applicants respectfully submit that the claims should not be limited by reciting that the incorporated reduction domains be different from that which was deleted, as suggested by the Examiner.

Turning to the §112, second paragraph rejection of claim 19, claim 19 has been amended so as to no longer make reference to claim 9. Accordingly, this ground of rejection has been overcome.

In view of the amendments presented herewith and the foregoing remarks, Applicants respectfully request the withdrawal of the rejection of claims 1, 2, 4-19, and 28 under 35 U.S.C. §112, second paragraph.

CLAIMS 1, 2, 4-13, 18, 19, and 28 AS AMENDED AND CLAIMS 14-17 MEET THE ENABLEMENT REQUIREMENT OF 35 U.S.C. 112, FIRST PARAGRAPH

In stating the rejection of claims 1, 2, 4-19, and 28 under 35 U.S.C. 112, first paragraph based on alleged inadequate enablement, the Examiner acknowledges that the specification is enabling for nucleic acid molecules encoding

PKSs that contain polylinker regions that (a) correspond in the translation of the deleted portion of the PKS and (b) encode an appropriately sized peptide. It is the Examiner's position, however, that the specification does not reasonably provide enablement for nucleic acid molecules encoding PKSs that contain polylinker regions that (a) do not correspond in the translation of the deleted portion of the PKS and (b) do not encode an appropriately sized peptide.

The Examiner has suggested adding to the claims the conditions that the polylinker be an in-frame addition and that the polylinker be limited in size. Applicants, for their part, have amended claim 1 to recite that the polylinker is an in-frame addition. Applicants, however, respectfully disagree with the Examiner as to limiting the length of the polylinker.

It is evident from Applicants' specification that one utility of the addition of the polylinker to the PKS is to introduce reduction domains into the PKS. A skilled artisan would appreciate that the addition of the reduction domain to the polylinker often results in the deletion of a significant portion of the polylinker. Indeed, the instant application at page 13, lines 14-21 provides guidance for utilizing different restriction sites for the insertion of the reduction domains, should the desired product not be obtained. The utilization of different restriction sites would, in effect, alter the length of the polylinker remaining in the construct. In light of the foregoing, it is Applicants' position that the overall length of the inserted polylinker is clearly not a significant factor and the claims should not be unduly limited in this connection.

Applicants also take exception to the Examiner's assessment of the eight factors to be considered in determining whether undue experimentation is required. As noted in MPEP §2164.01(a):

> It is improper to conclude that a disclosure is not

> enabling based on an analysis of only one of the [eight] factors while ignoring one or more of the others. The examiner's analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole. (Citation omitted.)

Applicants submit that the instant claims cannot be considered unduly broad, artisans in the field of this invention are highly skilled, the state of the art is well developed, and the instant application provides numerous working examples and considerable guidance to practice the full scope of the invention. While some experimentation may be necessary in carrying out the instant invention, given the unpredictability inherent in recombinant DNA technology, the amount of experiments involved cannot reasonably be considered excessive or undue in light of the guidance provided in this application. Therefore, when all eight Wands factors are considered as a whole, it is beyond question that the claimed invention is fully enabled by the specification.

In summary, the scope of enablement provided to those of ordinary skill in the art by the disclosure of the present application is clearly commensurate with the scope of protection sought by the claims. It must be concluded, therefore, that the enablement requirement of §112 is satisfied in the present case. In re Moore, 169 U.S.P.Q. 236 (CCPA 1971).

In view of the foregoing remarks, Applicants respectfully request the rejection of claim 1, 2, 4-19, and 28 under 35 U.S.C. §112, first paragraph be withdrawn.

CONCLUSION

In view of the amendments presented herewith and the foregoing remarks, it is respectfully urged that the objections and rejections set forth in the February 25, 2003 Official Action be withdrawn and that this application be passed to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number given below.

Respectfully submitted,

DANN, DORFMAN, HERRELL AND SKILLMAN
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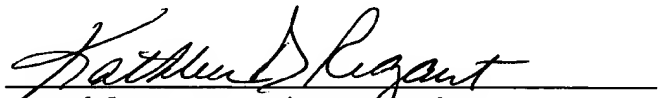
By 
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